

Appl. No. 09/975,317
Amendment dated: November 16, 2004
Reply to OA of: July 16, 2004

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

Claims 1-74(canceled).

75(new). A method of distinguishing viable myocardial tissue from necrotic (infarcted) tissue, said method comprising administering to said body a physiologically acceptable manganese complex or salt thereof at a dosage of 0.001 to 0.2 mmol/kg bodyweight, within a period of from 3 to 6 hours following administration of said complex or salt thereof subjecting said body to a magnetic resonance imaging procedure capable of generating images with time intervals of less than 0.5 seconds and thereafter providing a series of images of the myocardium of said body and distinguishing viable myocardial tissue from infarcted tissue; with the proviso that said manganese complex or salt thereof is the only contrast agent administered in said method.

76(new). A method as claimed in claim 75 wherein said magnetic resonance imaging procedure is one capable of generating images with time intervals of less than 100 milliseconds.

77(new). A method as claimed in claim 75 wherein said imaging procedure is a gradient echo or echo planar imaging procedure.

78(new). A method as claimed in claim 77 wherein said imaging procedure is an inversion recovery echo planar imaging procedure.

79(new). A method as claimed in claim 77 wherein said imaging procedure is one in which TI (inversion time) is 100 to 800 msec.

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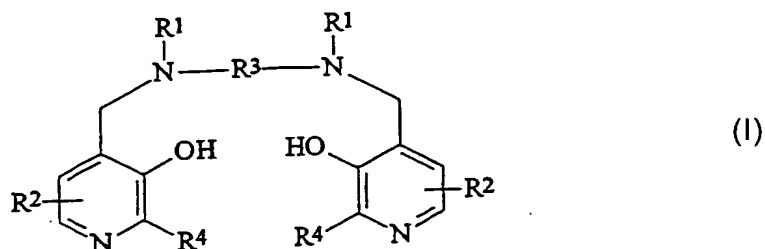
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80(new). A method as claimed in claim 75 wherein said manganese complex or salt thereof is administered at a dosage of 0.005 to 0.2 mmol/kg bodyweight.

81(new). A method as claimed in claim 80 wherein said manganese complex or salt thereof is administered at a dosage of 0.01 to 0.05 mmol/kg bodyweight.

82(new). A method as claimed in claim 75 wherein said manganese complex is a manganese chelate complex having a K_a value of from 10^7 to 10^{25} .

83(new). A method as claimed in claim 82 wherein said manganese chelate comprises a chelating compound of formula I:



or a salt thereof

(wherein in formula I

each R^1 independently represents hydrogen or $-\text{CH}_2\text{COR}^5$;

R^5 represents hydroxy, optionally hydroxylated alkoxy, amino or alkylamido;

each R^2 independently represents a group XYR^6 ;

X represents a bond, or a C_{1-3} alkylene or oxoalkylene group optionally substituted by a group R^7 ;

Y represents a bond, an oxygen atom or a group NR^6 ;

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R^6 is a hydrogen atom, a group COOR^8 , an alkyl, alkenyl, cycloalkyl, aryl or aralkyl group optionally substituted by one or more groups selected from COOR^8 , CONR^8_2 , NR^8_2 , OR^8 , $=\text{NR}^8$, $=\text{O}$, $\text{OP}(\text{O})(\text{OR}^8)\text{R}^7$ and OSO_3M ;

R^7 is hydroxy, an optionally hydroxylated, optionally alkoxyated alkyl or aminoalkyl group;

R^8 is a hydrogen atom or an optionally hydroxylated, optionally alkoxyated alkyl group;

M is a hydrogen atom or one equivalent of a physiologically tolerable cation;

R^3 represents a C_{1-8} alkylene group, a 1,2-cycloalkylene group, or a 1,2-arylene group; and

each R^4 independently represents hydrogen or C_{1-3} alkyl).

84(new). A method as claimed in claim 83 wherein in formula I:

R^5 is hydroxy, C_{1-8} alkoxy, ethylene glycol, glycerol, amino or C_{1-8} alkylamido;

X is a bond or a group selected from CH_2 , $(\text{CH}_2)_2$, CO , CH_2CO , $\text{CH}_2\text{CH}_2\text{CO}$ or CH_2COCH_2 ;

Y is a bond;

R^6 is a mono- or poly(hydroxy or alkoxyated) alkyl group or a group of the formula $\text{OP}(\text{O})(\text{OR}^8)\text{R}^7$; and

R^7 is hydroxy or an unsubstituted alkyl or aminoalkyl group.

85(new). A method as claimed in claim 83 wherein in formula I, R^3 is ethylene and each group R^1 represents $-\text{CH}_2\text{COR}^5$ in which R^5 is hydroxy.

86(new). A method as claimed in claim 83 in which the compound of formula I is N,N'-bis-(pyridoxal-5-phosphate)-ethylenediamine-N,N'-diacetic acid (DPDP) or N,N'-dipyridoxyl-ethylenediamine-N,N'-diacetic acid (PLED).

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87(new). A method as claimed in claim 82 wherein said chelate complex is a complex of a linear, branched or macrocyclic chelant selected from polyaminopolycarboxylic acid chelants and carboxylic acid derivatives thereof.

88(new). A method as claimed in claim 75 wherein said magnetic resonance imaging procedure is carried out within a period of up to 6 hours after the administration of said complex or salt thereof to said body.

89(new). A method as claimed in claim 75 wherein the contrast medium further comprises calcium chelate complexes.

90(new). A method as claimed in claim 75 wherein the contrast medium further comprises calcium or sodium salts.

91(new). A method as claimed in claim 90 wherein the calcium salt comprises calcium chloride, calcium ascorbate, calcium gluconate or calcium lactate.

92(new). A method as claimed in claim 75 wherein the contrast medium further comprises physiologically compatible buffers.

93(new). A method as claimed in claim 75 wherein the contrast medium further comprises an antioxidant such as ascorbic acid or a reducing sugar.

94(new). A method of distinguish viable myocardial tissue from necrotic (infarcted) tissue a human or non-human body, said method comprising administering to said body a contrast medium comprising a physiologically acceptable manganese chelate complex, subjecting said body to a magnetic resonance imaging procedure capable of generating images with time intervals of less than 0.5 seconds and thereafter providing a series of images of the myocardium of said body whereby to identify regions

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of abnormal blood flow, wherein said complex has a K_a value of from 10^7 to 10^{25} and is a complex of a chelant selected from the group consisting of N,N,N',N'',N'''-diethylenetriaminepentaacetic acid (DTPA) and 6-carboxymethyl-3,9-bis(methylcarbamoyl-methyl)-3,6,9-triazaundecanedioic acid (DTPA-BMA); with the proviso that said manganese complex or salt thereof is the only contrast agent administered in said method.

95(new). A method of discriminating between reversibly and irreversibly injured myocardial tissue, said method comprising administering to said body a physiologically acceptable manganese complex or salt thereof at a dosage of 0.001 to 0.2 mmol/kg bodyweight, subjecting said body to a magnetic resonance imaging procedure capable of generating images with time intervals of less than 0.5 seconds and thereafter providing a series of images of the myocardium of said body and discriminating reversibly from irreversibly injured tissue; with the proviso that said manganese complex or salt thereof is the only contrast agent administered in said method.